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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,746	10/01/2001	Maurice Zauderer	1821.0060001/EKS/AJK	3613

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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/966,746	ZAUDERER, MAURICE	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication app ars on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 8, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying immunogenic gene products, does not reasonably provide enablement for a method of identifying therapeutic gene products. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims are not enabled because determining what compounds are immunogenic does not mean that the compounds are therapeutic. In order to show that a compound is therapeutic, the practitioner must run further tests to determine which of the immunogenic particles may be used to treat or inhibit the target infection. Because the method does not include such a step, the method is not enabled for screening for therapeutics.

3. Claims 8, and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the specification, the applicant has disclosed the use of the method for identifying immunogens through differential expression of gene products between healthy and infected cells. However, the applicant has not described the identification of

immunogens through identifying gene products differentially expressed between adult and embryonic cells. Nor has the applicant shown that there are such immunogens to infectious diseases to be found or what type of gene products may constitute such immunogens to infectious diseases. It is not sufficient to define protein solely by its principal biological property, i.e. being expressed during embryogenesis, and not expressed during adulthood unless infected by a microorganism, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any protein with that biological property. Reciting antigens (which are generically known to exist) in a method claim, in the absence of knowledge as to the structure of antigens having the desired biological property consists of, is not a description of those antigens. Thus, claims to all proteins that have a desired biological property, without defining the structure of such proteins, do not comply with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1- 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In each of the method claims1, 8 and 9, the described method includes both a step of screening an identified host cell gene products for immunogenicity, and determining which of said host cell gene products are immunogenic. It is unclear why these are considered separate steps. Screening products for immunogenicity inherently determines whether those products are

immunogenic. It is therefore unclear whether the same step is required twice, or whether some other action is intended in the determining immunogenicity step.

6. Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the claims starts with an introduction stating "the method of [the claim from which it depends], comprising..." The claims then list all of the steps that were in the preceding claim, and those steps that are new. It is unclear whether the repeating of the steps in the preceding claim requires that the steps be carried out twice. It would be clearer if the claims were phrased "the method of [the preceding claim], further comprising the steps of..."

7. The term "low level in uninfected cells" in claim 2 is a relative term that renders the claim indefinite. The term "low level" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. However, the language "are expressed at a lower level in uninfected cells than in infected cells of the same type."

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Number 5,721,351, issued to Douglas Adam Levinson (the 351 patent). Claim 1 describes a

method of screening for therapeutics for infectious diseases comprising 1) identifying host cell gene products either up regulated during, or expressed only upon, infection, 2) screening the gene products for immunogenicity, and 3) determining which of said cell products are immunogenic. For the purposes of this rejection, the two later steps are part of a single process of determining immunogenicity.

The 351 patent discloses a method of identifying compounds that modulate expression of genes or the activity of gene products involved in helper T-Cell (TH cell) related disorders. Patent, col. 5, lines 43-49. The patent further teaches that some of these modulators may be used in methods of treatment of TH related disorders. Col. 5, lines 49-54. The disclosed method centers on the identification of differentially expressed gene products in TH cell. Col. 13, lines 17-22. Such variations in expression may either be detectable in cells of one state, and not in another, or may be of differing expression levels in each state (normal and with the TH cell disorder). Col. 14, lines 27-34. These differences may occur between normal TH cells, and those wherein the TH cells are present with a TH cell related disorder. E.g., col. 14 lines 18 and 33-34, and col. 16, lines 26-41. Among the TH cell related disorders that the method may be applied to are those wherein the disorder is related to a viral or bacterial infection, including an HIV infection. Col, 16, lines 39-41. Thus, the 351 patent discloses a method of identifying compounds that are either expressed only upon infection, or are variably expressed between normal and infected states (this inherently includes both *up regulation* and down regulation in the infected cells), and the use of some of the identified compounds as therapeutics.

Further, the patent teaches methods wherein the identified gene products are screened to determine their ability to ameliorate immune disorder symptoms. Col. 45, lines 3-6. Because the

patent teaches that some of the identified molecules may be used as therapeutics (col. 5, lines 49-53), and teaches the identification of gene products variably expressed in TH cells and the identification of such molecules that modulate the TH cell phenotypes (col. 45, above), it also inherently teaches a method of screening for immunogenic gene products. The application states that immunogenicity includes helper T-cell responses. The above described method deals with the identification of molecules that modulate TH cell phenotypes. This would inherently include the response of the cells to antigens and its environment. Thus, claim 1 is anticipated.

Claims 2 and 3 are anticipated because, as stated above, the patent teaches the identification of differentially expressed gene products between cells wherein the variations in expression may either be detectable in cells of one state, and not in another, or may be of differing expression levels in each state. Col. 14, lines 27-34. The patent therefore teaches that the gene products may be either up-regulated or down-regulated between the normal and infected states, and may not be expressed at all in the normal (uninfected) cells. Claim 4 is anticipated because among the TH cell disorders for which the method may be applied is HIV. Col. 1, line 23.

Finally, claim 7 is anticipated because, among the methods of identifying differentially expressed gene products disclosed by the patent, the 351 patent discloses the use of subtractive hybridization. Col. 18, lines 1-11. As claim 7 is limiting claim 1 to methods wherein the differentially expressed gene products are identified by subtractive hybridization, the claim is anticipated by the patent for the reason given above, and because it teaches the use of this technique.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over the 351 patent in light of the teachings of U.S. Patent Number 6,004,755 (issued to Bruce Wang, and hereinafter the 158 patent) relating to the use of microarrays to identify differentially expressed genes. Claim 5 adds to claim 1 the limitation that the identification of differentially expressed genes be done using ordered microarrays.

The teachings of the 351 patent are described above. The 158 patent teaches various method of gene expression analysis using microarrays. Among other types of analysis, the patent teaches that microarrays may be used for differential expression analysis. Thus, it would have been obvious to one of ordinary skill in the art to use an ordered microarray system to identify differentially expressed gene products.

12. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over the 351 patent in light of U.S. Patent number 6,312,731(the 731 patent), issued to Staas et al. and U.S. Patent Number 5,846,827 (the 827 patent), issued to Celis et al. Claim 5 describes the method of claim 1 wherein the screening for immunogenicity comprises screening for a cytotoxic T-cell (CTL) response to the identified gene product.

The teachings of the 351 patent are described above. The other two references each illustrate that a CTL response is one indication of the immunogenicity of a molecule. See, the

731 patent, col. 2, lines 20-35 (indicating that a CTL response is a form of immunogenic response); and the 827 patent, col. 3, lines 60-67 (defining an immunogenic peptide as one capable of inducing a CTL response). Together, the references establish that one of ordinary skill in the art would know that one indication of a molecules ability to act as an immunogen is the ability of that molecule to induce a CTL response. Therefore, claim 5 is obvious when seen in light of the 351 patent's teachings, and fact that one of ordinary skill in the art would have known to use a CTL response as an indication of immunogenicity.

13. Claims 1, 2, and 3 are also rejected under 35 U.S.C. 103(a) as being obvious over the 351 patent and U.S. Patent Numbers 6,399,328 (the 328 patent- issued to Vournakis et al.), and 6,312,909 (the 909 patent- issued to Andrew J. Shyjan). Claim 1 and the teachings of the 351 patent are described above. Both of the other patents describe a method of identifying tumor or cancer associated gene products through differential expression. See. 328 patent, col. 4-5, and the 909 patent, col. 3, lines 58-64. Further, both of the patents also indicate that the gene products so identified may then be used to devise new treatments or yield new targets for treating cancers and tumors. 328 patent, col. 5, lines 23-31; 909 patent, col. 4, lines 10-15. As such, each indicates that, having identified potential therapeutics, one skilled in the art should then assay these identified gene products for immunogenic properties.

The 909 patent further teaches that the differential expression analysis may be used to identify two separate types of genes. Col. 4, lines 46-53. First, those that are expressed only in the presence of the disease being studied. Col. 4, lines 54-66 (describing the fingerprint genes as those that may be used as prognostic or diagnostic markers for tumor disorders). Secondly, there are target genes that are expressed at different levels in healthy and unhealthy cells. Col. 5, lines

6-21. Thus, the patent teaches the two types of differentially expressed genes that are described in claims 2 and 3.

Although the 328 and 909 patents are not concerned with infectious diseases as is required by claim 1, they are relevant to the claimed invention in that they show that the methods of claims 1-3 are known in the art as applicable to large number of unrelated diseases- both infectious and otherwise. As such, the claimed methods would obvious to one of ordinary skill in the art to the extent that the method is not directly anticipated by the 351 patent.

Conclusion

14. The following art reference is made of record although it is not relied upon in a rejection of the claims: Tanka et al., PNAS 97:9127-9132. This reference indicates that differential expression of gene products between embryonic and adult tissues may be useful in identifying compounds involved in tumorigenesis. This reference is considered pertinent to applicant's disclosure because it indicates that a method involving identification of gene products expressed in embryonic, but not adult, tissues would have been obvious to one of ordinary skill in the art where the disease to be treated was cancer or tumor related. However, as the applicant is claiming a method dealing with infectious diseases (i.e. those caused by microorganisms as identified in the specification on p. 8, lines 5-7), this reference in not applicable against the applicants claims. It is relevant only as an indication of the closest art.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
June 27, 2002

James C. Housel 7/1/02

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